

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	5	aerothricin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:39			0
2	BRS	L2	1190	mycoses	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:41			0
3	BRS	L3	2	aerothricin same mycoses	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:41			0
4	BRS	L4	2	kohchi adj masami.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:42			0
5	BRS	L5	7	masubuchi adj kazunao.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:42			0
6	BRS	L6	241	murata adj takeshi.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:42			0
7	BRS	L7	156	okada adj takehiro.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:43			0
8	BRS	L8	35	shimma adj nobuo.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:43			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
9	BRS	L9	5	(4 or 5 r 6 or 7 or 8) and 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/06 06:44			0

FILE 'MEDLINE' ENTERED AT 06:48:49 ON 06 JAN 2004

FILE 'CAPLUS' ENTERED AT 06:48:49 ON 06 JAN 2004  
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FILE 'SCISEARCH' ENTERED AT 06:48:49 ON 06 JAN 2004  
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FILE 'AGRICOLA' ENTERED AT 06:48:49 ON 06 JAN 2004

=> s aerothricin  
L1 16 AEROTHRICIN

=> s mycoses  
L2 21346 MYCOSES

=> s l1 (p) l2  
L3 3 L1 (P) L2

=> duplicate remove l3  
DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L3  
L4 1 DUPLICATE REMOVE L3 (2 DUPLICATES REMOVED)

=> d l4 1 ibib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 2002:136646 CAPLUS  
TITLE: Aerothricins: a new class of .beta.-glucan inhibitors  
AUTHOR(S): Anon.  
SOURCE: Expert Opinion on Therapeutic Patents (2002), 12(2),  
315-318  
CODEN: EOTPEG; ISSN: 1354-3776  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; Miscellaneous  
LANGUAGE: English

AB Two patent applications assigned to Basilea Pharmaceutica describe  
\*\*\*aerothricin\*\*\* natural product mols. and a large series of  
semi-synthetic mols. claimed as antifungal drugs that inhibit the  
.beta.-1,3-D-glucan component of the cell wall. The semi-synthetic mols.,  
considerably larger than the previous hexapeptide echinocandin and  
pneumocandin mols., contain various basic amino acids and a large series  
of aminoalkyl groups and are presumably more water-sol. than the natural  
product \*\*\*aerothricins\*\*\*. Overall, the antifungal in vitro  
susceptibility results compared favorably with other .beta.-glucan  
inhibitors. Results are also presented for select compds. in mouse models  
of \*\*\*mycoses\*\*\* that indicate good activity. One of the applications  
is largely focused on formulations of pharmacol.-active cyclic peptides  
with absorption enhancers delivered by the intranasal route and provides  
pharmacokinetic data in cynomolgous monkeys in support of the claims.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s kohchi masubuchi/au  
L5 0 KOHCHI MASUBUCHI/AU

=> s kohchi masami/au  
L6 10 KOHCHI MASAMI/AU

=> s masubuchi kazunao/au  
L7 18 MASUBUCHI KAZUNAO/AU

=> s murata takeshi/au  
L8 202 MURATA TAKESHI/AU

=> s okada takehiro/au

L9 51 OKADA TAKEHIRO/AU

=> s shimma nobuo/au  
L10 100 SHIMMA NOBUO/AU

=> s 16 or 17 or 18 or 19 or 110  
L11 340 L6 OR L7 OR L8 OR L9 OR L10

=> s 111 and 11  
L12 4 L11 AND L1

=> duplicate remove 112  
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L12  
L13 4 DUPLICATE REMOVE L12 (0 DUPLICATES REMOVED)

=> 'd 113 1-4 ibib abs  
'D IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d 113 1-4 ibib abs

L13 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2003:67242 BIOSIS  
DOCUMENT NUMBER: PREV200300067242  
TITLE: Cyclic compounds.  
AUTHOR(S): Aoki, Masahiro [Inventor, Reprint Author]; \*\*\*Kohchi,\*\*\*  
\*\*\* Masami\*\*\* [Inventor]; \*\*\*Masubuchi, Kazunao\*\*\*  
[Inventor]; Mizuguchi, Eisaku [Inventor]; \*\*\*Murata,\*\*\*  
\*\*\* Takeshi\*\*\* [Inventor]; Ohkuma, Hiroaki [Inventor];  
\*\*\*Okada, Takehiro\*\*\* [Inventor]; Sakaitani, Masahiro  
[Inventor]; \*\*\*Shimma, Nobuo\*\*\* [Inventor]; Watanabe,  
Takahide [Inventor]; Yanagisawa, Mieko [Inventor]; Yasuda,  
Yuri [Inventor]  
CORPORATE SOURCE: Chigasaki, Japan  
ASSIGNEE: Basilea Pharmaceutica AG, Binningen, Switzerland  
PATENT INFORMATION: US 6489440 December 03, 2002  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Dec. 3, 2002) Vol. 1265, No. 1.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
ISSN: 0098-1133 (ISSN print).  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 29 Jan 2003  
Last Updated on STN: 29 Jan 2003

AB The present invention relates to novel \*\*\*Aerothricins\*\*\* represented  
by the Formula (I), ##STR1## wherein R1, R2, R3, R4, R5, X, Y, Z, and m  
are as defined in Claim 1; and pharmaceutically acceptable salts thereof.  
The present invention also relates to a pharmaceutical composition  
comprising an \*\*\*Aerothricin\*\*\* of the Formula (I) and a  
pharmaceutically acceptable carrier. Furthermore, the present invention  
relates to the use of such \*\*\*Aerothricins\*\*\* for the preparation of  
medicaments, as well as to processes and intermediates for the preparation  
of the \*\*\*Aerothricins\*\*\* of the Formula (I).

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:545715 CAPLUS  
DOCUMENT NUMBER: 135:137714  
TITLE: Preparation of \*\*\*aerothricins\*\*\*, novel cyclic  
compounds having antifungal activity  
INVENTOR(S): \*\*\*Kohchi, Masami\*\*\*; \*\*\*Masubuchi, Kazunao\*\*\*  
; \*\*\*Murata, Takeshi\*\*\*; \*\*\*Okada, Takehiro\*\*\*  
; \*\*\*Shimma, Nobuo\*\*\*  
PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053322	A2	20010726	WO 2001-EP251	20010111

WO 2001053322 A3 20020131  
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
AU 2001025148 A5 20010731 AU 2001-25148 20010111  
EP 1254161 A2 20021106 EP 2001-900419 20010111  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
BR 2001007609 A 20021119 BR 2001-7609 20010111  
JP 2003520804 T2 20030708 JP 2001-553794 20010111  
US 2001031728 A1 20011018 US 2001-760949 20010116  
PRIORITY APPLN. INFO.: EP 2000-100807 A 20000117  
WO 2001-EP251 W 20010111  
OTHER SOURCE(S): MARPAT 135:137714  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB \*\*\*Aerothricin\*\*\* derivs. I [R1 = N-(3-aminopropyl)-N-[(2S)-2,5-diaminovaleryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N,N-bis(2-aminopropyl)amino]valeryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N-(3-aminopropyl)amino]valeryl]amino, N-(2-aminoethyl)-N-[5-amino-2-[N,N-bis(2-aminopropyl)amino]valeryl]amino or ornithylornithylamino; R2 = H, Me; R3 = H, OH] or pharmaceutically acceptable salts were prepd. for use as fungicides. Thus, \*\*\*aerothricin\*\*\* 3 (I; R1 = NH2, R2 = R3 = H), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions, was treated with acrylonitrile in MeOH in the presence of Et3N to give \*\*\*aerothricin\*\*\* 120 (I; R1 = NHCH2CH2CN, R2 = R3 = H). Coupling of \*\*\*aerothricin\*\*\* 120 with Boc-L-Orn(Boc)-OH (Boc = tert-butoxycarbonyl, Fmoc = 9-fluorenylmethoxycarbonyl) in DMF using BOP reagent, HOBT hydrate and N-ethyl-diisopropylamine, followed by deprotection with TFA and hydrogenolysis over 10% Pd on charcoal, afforded \*\*\*aerothricin\*\*\* 132 [I; R1 = L-Orn-N[(CH2)3NH2], R2 = R3 = H]. The \*\*\*aerothricins\*\*\* of formula I exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are much less cytotoxic to hepatocytes than the known cyclic peptide derivs. WF11243 and LY303366.

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:545525 CAPLUS  
DOCUMENT NUMBER: 135:157672  
TITLE: Cyclic peptide compositions for nasal administration  
INVENTOR(S): Horii, Ikuo; Kobayashi, Kazuko; \*\*\*Shimma, Nobuo\*\*\*  
; Yanagawa, Akira  
PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
SOURCE: PCT Int. Appl., 117 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052894	A2	20010726	WO 2001-EP163	20010109
WO 2001052894	A3	20020131		
W:		AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
EP 1251827	A2	20021030	EP 2001-909587	20010109
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,		

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 BR 2001007764 A 20021112 BR 2001-7764 20010109  
 JP 2003535042 T2 20031125 JP 2001-552941 20010109  
 US 2001038824 A1 20011108 US 2001-765846 20010119  
 PRIORITY APPLN. INFO.: EP 2000-101057 A 20000120  
 WO 2001-EP163 W 20010109

OTHER SOURCE(S): MARPAT 135:157672

AB The present invention relates to a nasal compn. of physiol. active cyclic peptides and salts that are prepd. by homogeneously dispersing an active cyclic peptide such as antifungal cyclic peptides ( \*\*\*aerothricin\*\*\* , echinocandin analogs, pneumocandin analogs, and aureobasidin), antibacterial cyclic peptides (e.g., vancomycin, daptomycin), cyclosporin A, lanreotide, vapreotide, vasopressin antagonist and eptifibatide in a unique carrier. The powdery or cryst. carrier contains a water insol. polyvalent metal carrier, or org. carrier having a mean particle size of 20-500 .mu.m, in the presence or absence of an absorption enhancer and by homogeneously adsorbing onto the carrier, and its use for therapeutic treatment of disease such as systemic fungal infections by intranasal administration. The compn. can be nasally administered in a powder form. Thus, 201 mg \*\*\*Aerothricin\*\*\* 133 and 599 mg CaCO3 (mean particle size: 40-60 .mu.m) were mixed well. Then, 200 .mu.L water was added, and mixing was continued until the mixt. became a paste and the resulting pasty solid was freeze-dried at -50.degree., and further dried at 300.degree. for 3 h in vacuo. After large particles in the dry powder were broken into small particles, 8 mg of calcium stearate was added and the mixt. was passed through 180-.mu.m-mesh. \*\*\*Aerothricin\*\*\* 133 was synthesized by a series of steps.

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:84834 CAPLUS

DOCUMENT NUMBER: 132:137733

TITLE: Preparation of new antifungal agents, cyclic  
 \*\*\*aerothricin\*\*\* analogs, for treatment of  
 infectious diseases caused by pathogenic  
 microorganisms

INVENTOR(S): Aoki, Masahiro; \*\*\*Kohchi, Masami\*\*\* ;  
 \*\*\*Masubuchi, Kazunao\*\*\* ; Mizuguchi, Eisaku;  
 \*\*\*Murata, Takeshi\*\*\* ; Ohkuma, Hiroaki; \*\*\*Okada,\*\*\*  
 \*\*\*Takehiro\*\*\* ; Sakaitani, Masahiro; \*\*\*Shimma,\*\*\*  
 \*\*\*Nobuo\*\*\* ; Watanabe, Takahide; Yanagisawa, Mieko;

Yasuda, Yuri

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005251	A1	20000203	WO 1999-EP5235	19990722
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335394	AA	20000203	CA 1999-2335394	19990722
AU 9951630	A1	20000214	AU 1999-51630	19990722
AU 754285	B2	20021114		
BR 9912367	A	20010502	BR 1999-12367	19990722
EP 1100816	A1	20010523	EP 1999-936588	19990722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525263	T2	20020813	JP 2000-561207	19990722
US 6489440	B1	20021203	US 1999-360476	19990723
PRIORITY APPLN. INFO.:			EP 1998-113744	A 19980723
			EP 1999-107637	A 19990416
			WO 1999-EP5235	W 19990722

OTHER SOURCE(S): MARPAT 132:137733

GI

/ Structure 1 in file .gra /

AB Novel antifungal \*\*\*aerothricins\*\*\* I [R1 = guanidino, trialkylammonio, NR10R11, NR15COR14, NR15COCH(NR10R11)R13 (Q), NHCCHR13NHCOCH(NH2)R13, N[(CH2)nQ]2, N[(CH2)nQ][COCH(NR10R11)R13], or NR15COR12, where n = 2-5, R10, R11 = H, heteroaryl or mono- or diaminoheteroaryl, alkyl optionally substituted with one or more amino groups, aminoalkyl, cyano, guanidino, nitrogen-contg. heterocycle(s) or Ph group(s) contg. an amino, amidino or guanidino group, R12 is tetrahydro-2-pyrrolyl optionally substituted at N by R10 and by an amino group, R13 is a residue from natural or unnatural amino acids, R14 is alkyl substituted with one or more amino, guanidino, nitrogen contg. heterocycle or Ph group contg. an amino, amidino, or guanidino group, and R15 = H or R14-like group; R2 = H, HOSO2, alkyl or alkenyl optionally substituted with acyl, carbamoyl, amino, mono- or dialkylamino; R3 = H, OH, NO2, NH2, acylamino, (alkylcarbamoyl)amino, carboxyl, alkoxy, alkoxy carbonyl, (un)substituted alkyl, alkenyl, or alkynyl; R4 = alkyl, alkenyl, alkoxy or alkenyloxy optionally substituted with alkyl, aryl, cycloalkyl or F; R5 = CONH2, CN, CH2NH2; X is a single bond, aryl, biphenyl, terphenyl optionally contg. one or more heteroatom(s) and/or substituted with halo or alkyl; Y is a single bond, CH2, CH(alkyl), CONH, CON(alkyl); Z = O, NH, alkylamino; m = 0-4 (with provisos)] and pharmaceutically acceptable salts were prepd. Numerous processes for the prepn. of \*\*\*aerothricins\*\*\* of formula I are described. Thus, \*\*\*aerothricin\*\*\* 3 [I; R1 = NH2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me] (WF11243), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions in aq. medium, was treated with (2-oxoethyl)carbamic acid tert-Bu ester in MeOH in the presence of sodium cyanoborohydride and acetic acid to afford \*\*\*aerothricin\*\*\* 111 [I; R1 = N(CH2CH2NH2)2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me]. The \*\*\*aerothricins\*\*\* of formula I as well as pharmaceutically acceptable salts exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are less cytotoxic to hepatocytes than the known cyclic peptide derivs., e.g., WF11243.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 06:48:49 ON 06 JAN 2004

L1	16 S AEROTHRICIN
L2	21346 S MYCOSES
L3	3 S L1 (P) L2
L4	1 DUPLICATE REMOVE L3 (2 DUPLICATES REMOVED)
L5	0 S KOHCHI MASUBUCHI/AU
L6	10 S KOHCHI MASAMI/AU
L7	18 S MASUBUCHI KAZUNAO/AU
L8	202 S MURATA TAKESHI/AU
L9	51 S OKADA TAKEHIRO/AU
L10	100 S SHIMMA NOBUO/AU
L11	340 S L6 OR L7 OR L8 OR L9 OR L10
L12	4 S L11 AND L1
L13	4 DUPLICATE REMOVE L12 (0 DUPLICATES REMOVED)

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COST IN U.S. DOLLARS

SINCE FILE  
ENTRY  
32.49

TOTAL  
SESSION  
32.70

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE  
ENTRY  
-2.77

TOTAL  
SESSION  
-2.77

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